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(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
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CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
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KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
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For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: COMPOSITION AND METHOD FOR NERVE REGENERATION

(57) Abstract: The present invention provides a pharmaceutical composition and method for regenerating nerves and treating neu-
rological diseases based on nerve regeneration. The present invention employs a substance, such as Pep5, PKC, IP3, Rho, Rho GDI,
Rho kinase, or the like, which are involved in a p75 signal transduction pathway, or an agent capable of specifically interacting with
any of these substances to block or suppress the p75 signal transduction pathway, thereby stopping inhibition of nerve regeneration.
As a result, nerve regeneration is resumed. The present invention is also the first to disclose that the PTD domain is useful as an
agent for nerve regeneration.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K7/08 A61K38/10 C12N15/11 G01N33/50 C12N15/62
A01K67/027 C12N15/10 A61P25/28

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K A61K C12N G01N A01K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, EMBASE, BIOSIS, WPI Data, PAJ, CHEM ABS Data, PASCAL

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	<p>YAMASHITA TOSHIHIDE ET AL: "The p75 receptor acts as a displacement factor that releases Rho from Rho-GDI." NATURE NEUROSCIENCE. MAY 2003, vol. 6, no. 5, May 2003 (2003-05), pages 461-467, XP002295642 ISSN: 1097-6256</p> <p>the whole document</p> <p>----- -/--</p>	<p>1-10, 41-48, 50-58, 60,66, 71-75, 80,86, 89, 91-93, 97-115</p>

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

10 September 2004

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19. 01. 2005

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Fayos, C

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 International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ILAG L L ET AL: "Selection of a peptide ligand to the p75 neurotrophin receptor death domain and determination of its binding sites by NMR." BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS. 5 FEB 1999, vol. 255, no. 1, 5 February 1999 (1999-02-05), pages 104-109, XP002295643 ISSN: 0006-291X	1-4,61, 66,72, 73,75, 80,86, 87,89, 91-93, 97,98, 100-102, 105-107
Y	abstract page 106, column 1, paragraph 3 - column 2, paragraph 1	1-10, 41-48, 50-58, 60,66, 71-75, 80,86, 89, 91-93, 97-115
X	ILAG, LEOPOLD LUNA: "Biochemical and biophysical aspects of molecular recognition and signalling by neurotrophins" DOKTORSÄVHANDLING VID KAROLINSKA INSTITUET, 'Online! 7 November 1997 (1997-11-07), XP002295644 Retrieved from the Internet: URL:http://diss.kib.ki.se/1997/1997110711a g/> 'retrieved on 2004-09-09!	1-4,61, 66,72, 73,75, 80,86, 87,89, 91-93, 97,98, 100-102, 105-107
Y	abstract In particular the last two paragraphs ----- -/--	1-10, 41-48, 50-58, 60,66, 71-75, 80,86, 89, 91-93, 97-115

INTERNATIONAL SEARCH REPORT

International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WONG SCOTT T ET AL: "A p75(NTR) and Nogo receptor complex mediates repulsive signaling by myelin-associated glycoprotein." NATURE NEUROSCIENCE. DEC 2002, vol. 5, no. 12, December 2002 (2002-12), pages 1302-1308, XP002295645 ISSN: 1097-6256 cited in the application abstract	1-10, 41-48, 50-58, 60,66, 71-75, 80,86, 89, 91-93, 97-115
X	page 1306, column 1, paragraph 3 - column 2	61,66, 72,73, 75,80, 86,87, 89, 91-93, 97,98, 100-102, 105-107
X	US 6 242 416 B1 (GILCHREST BARBARA A ET AL) 5 June 2001 (2001-06-05)	61,66, 72,73, 75,80, 86,87, 89, 91-93, 97,98, 100-102, 105-107
Y	column 2, line 40 - line 56	1-10, 41-48, 50-58, 60,66, 71-75, 80,86, 89, 91-93, 97-115
	column 5, line 9 - line 55 claims 1-10	
A	WOOLF C J BLOECHLINGER S: "It takes more than two to Nogo" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 297, 16 August 2002 (2002-08-16), pages 1132-1134, XP002957213 ISSN: 0036-8075	1-10, 41-48, 50-58, 60,66, 71-75, 80,86, 89, 91-93, 97-115
	page 1132, column 3, line 10 - line 12 page 1133; figure page 1133, column 3, paragraph 2 - paragraph 3	
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International Application No
PCT/JP2004/004385

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>YAMASHITA TOSHIHIDE ET AL: "The p75 receptor transduces the signal from myelin-associated glycoprotein to Rho." THE JOURNAL OF CELL BIOLOGY. 13 MAY 2002, vol. 157, no. 4, 13 May 2002 (2002-05-13), pages 565-570, XP002295646 ISSN: 0021-9525</p> <p>abstract the whole document</p>	<p>1-10, 41-48, 50-58, 60,66, 71-75, 80,86, 89, 91-93, 97-115</p>
Y	<p>WANG KEVIN C ET AL: "P75 interacts with the Nogo receptor as a co-receptor for Nogo, MAG and OMgp." NATURE. 7 NOV 2002, vol. 420, no. 6911, 7 November 2002 (2002-11-07), pages 74-78, XP001183135 ISSN: 0028-0836</p> <p>the whole document</p>	<p>1-10, 41-48, 50-58, 60,66, 71-75, 80,86, 89, 91-93, 97-115</p>
X	<p>WO 95/11253 A (BARRETT GRAHAM LESLIE ; INST MEDICAL W & E HALL (AU)) 27 April 1995 (1995-04-27)</p>	<p>61,66, 72,73, 75,80, 86,87, 89, 91-93, 97,98, 100-102, 105-107</p>
Y	<p>claims 1-49</p>	<p>1-10, 41-48, 50-58, 60,66, 71-75, 80,86, 89, 91-93, 97-115</p>
X	<p>BOTCHKAREV V A ET AL: "A new role for p75 neurotrophin receptor in hair follicle regression: Catagen retardation in p75NTR knockout mice and after p75NTR blockade by cyclic peptides" JOURNAL OF INVESTIGATIVE DERMATOLOGY, vol. 112, no. 4, April 1999 (1999-04), page 553, XP009036309 & 60TH ANNUAL MEETING OF THE SOCIETY FOR INVESTIGATIVE DERMATOLOGY; CHICAGO, ILLINOIS, USA; MAY 5-9, 1999 ISSN: 0022-202X abstract</p>	<p>115</p>

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/JP2004/004385

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>WO 01/19393 A (CORNELL RES FOUNDATION INC) 22 March 2001 (2001-03-22)</p> <p>page 8, line 30 - page 9, line 5</p> <p>page 14, line 17 - page 15, line 15 example 1 claims 1-13</p>	<p>5, 10, 41-48, 50-58</p>
Y	<p>SCHWARZE S R ET AL: "PROTEIN TRANSDUCTION: UNRESTRICTED DELIVERY INTO ALL CELLS?" TRENDS IN CELL BIOLOGY, ELSEVIER SCIENCE LTD, XX, vol. 10, no. 7, July 2000 (2000-07), pages 290-295, XP001135090 ISSN: 0962-8924 the whole document</p>	<p>5, 10, 41-48, 50-58</p>

INTERNATIONAL SEARCH REPORT

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 99-104, 108 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-10, 41-48(part), 50-58(part), 60(part), 61(part), 66(part), 72-74(part)
75(part), 80(part), 86-88(part), ...

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/JP2004/004385

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 6242416	B1	05-06-2001	US 2004254110 A1	16-12-2004
			US 2002051988 A1	02-05-2002
			AU 719038 B2	04-05-2000
			AU 2424597 A	22-10-1997
			EP 0890105 A1	13-01-1999
			JP 2000507828 T	27-06-2000
			CA 2250075 A1	09-10-1997
			WO 9737228 A1	09-10-1997
WO 9511253	A	27-04-1995	AU 689145 B2	26-03-1998
			AU 7984394 A	08-05-1995
			WO 9511253 A1	27-04-1995
			CA 2174425 A1	27-04-1995
			EP 0724589 A1	07-08-1996
			JP 9503512 T	08-04-1997
			US 6174869 B1	16-01-2001
			US 5837694 A	17-11-1998
WO 0119393	A	22-03-2001	AU 7577600 A	17-04-2001
			WO 0119393 A1	22-03-2001
			US 6485977 B1	26-11-2002